AMENDMENTS TO THE DRAWINGS

The attached one (1) Replacement Sheet of Figure 8 and three (3) Annotated Sheets of Figures 6-8 are submitted to replace Figures 6-8 (sheets 17/19 through 19/19) of the originally-filed drawing sheets. The drawings have been amended to delete Figures 6 and 7 and renumber Figure 8 as Figure 6. No new matter has been added.

REMARKS

Reconsideration is requested.

Claims 76-114 are pending. Claims 76-105 and 112-114 have been withdrawn from consideration. Claims 1-75, 107, 108 and 110 have been canceled, without prejudice. Claims 106, 109 and 111 are under active consideration.

The specification has been revised to include a revised specification and Figures, without prejudice.

Experiments using plexin B1 genes cloned into NIH3T3 cells were described in the specification as filed. In these experiments, expression of the plexinB1 gene was confirmed in these NIH3T3 cells after transfection by RT-PCR and sequencing. Transfected NIH3T3 cells were then used to assess anchorage independent growth (page 52 line 23 to page 53 line 2) and tumourigenicity in athymic nude mice (page 55 line 14 to page 56 line 9).

However, after the application was filed, subsequent analysis of the transfected NIH3T3 cells used in these experiments with antibodies showed that, although the wild type and mutant plexin B1 genes were expressed at the RNA level in the transfected NIH3T3 cells, little or no translation into protein was occurring. The transfected NIH3T3 cells therefore contained little or no plexinB1 protein and the experiments described in the specification which employ these cells therefore provide no information about the effect of wild type and mutant plexin B1 on anchorage independent growth or tumourigenicity.

In the light of this, the specification has been corrected to remove those parts which relate to these experiments.

No new matter has been added.

The substitute specification and drawings include a section title of Brief Description of the Drawings and the objected-to Figure 6 has been deleted from the specification. The specification is believed to be in compliance with the Rules and MPEP, which provides in § 601 suggestions for the preferred arrangement of the specification. Withdrawal of the objections to the specification and drawings are requested.

The Section 112, second paragraph, rejection of claims 106-111 is obviated by the above amendments. Withdrawal of the rejection is requested.

The Section 112, second paragraph, rejection of claims 107-109 is obviated by the above amendments. Claim 106 has been amended to specify that the listed positions refer to positions in the sequence of AB0007867.1. The applicants believe that the person of ordinary skill in the art will readily appreciate the metes and bounds of the claims and the location of the recited mutations in the plexinB1 sequence. Withdrawal of the rejection is requested.

To the extent not obviated by the above amendments, the Section 112, first paragraph "enablement", rejection is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following comments.

The Examiner is understood to believe that, although the A5653G plexin B1 mutant is shown to be present in prostate tumours, this mutant plexin B1 is also shown

to reduce tumorigenicity in vivo; that the ordinarily skilled person could not predictably know what change in the expression of the A5653G plexin B1 mutant would be important for affecting tumour formation and would not therefore be able to predictably identify and/or obtain an anti-cancer agent based on a change in expression of the A5653G plexin B1 mutant.

As described above, the transfected NIH3T3 cells used in the in vivo tumorigenicity experiments in fact produced little or no mutant or wild-type plexinB1 protein. The in vivo tumorigenicity experiments described in the specification therefore do not allow any conclusions to be drawn about the effect of wild type and mutant plexinB1 protein on tumourigenicity.

However, the applicant submit that the data set out in the originally-filed application on pages 51 line 16 to page 52 line 14, page 53 line 4 to page 55 line 13 and page 56 line 10 to page 56 line 26 show that the A5653G and other mutations in the plexinB1 coding sequence present in a high proportion of tumour samples and not present in healthy tissue samples and therefore display a strong positive correlation with the formation of breast and prostate tumours.

In the light of this strong positive correlation, the applicants believe that one of ordinary skill in the art would reasonably predict that a decrease in expression of the mutant plexin B1 would be important for reducing the formation of tumours and would therefore be able to predictably identify and/or obtain an anti-cancer compound based on a decrease in expression of the A5653G mutant and other mutant plexinB1 nucleic acids.

The Examiner is further understood to believe that one could not predictably extrapolate from prostate cancer to any tumour type without undue experimentation.

The applicants believe however that the data set out in the originally-filed application on pages 51 line 16 to page 52 line 14 and page 53 line 4 to page 55 line 13 show that the A5653G mutation and the other listed mutations in the plexinB1 coding sequence display a strong positive correlation with the formation of prostate tumours.

The applicants believe that the data set out in the originally-filed application on page 56 lines 10 to 26 show that the A5653G mutation and the other listed mutations in the plexinB1 coding sequence display a strong positive correlation with the formation of breast tumours.

A person of ordinary skill in the art could predictably extrapolate the described correlation between mutant plexin B1 and tumour formation to breast and prostate tumours without undue experimentation based on the information in the specification and known in the art.

The Examiner further understood to believe that that one of ordinary skill in the art would not predictably expect that all of the claimed mutants of plexin B1 are associated with cancer and thus an effect on their expression would allegedly not be predictably useful for identifying a compound as a putative anti-cancer agent.

The instant claims recite mutations located at specified positions in the coding sequence of plexinB1 which are identified by reference to the sequence of database and publicly available entry AB0007867.1. Mutations located at all of the specified positions are shown in the specification to correlate with prostate and/or breast cancer.

Furthermore, the applicants submit that mutations at these positions alter an amino acid in the encoded plexinB1 protein. Many of these amino acids are at sites which are conserved in evolution and therefore are likely to be important functionally. Moreover, the applicants submit that all the mutants studied to date alter cell function. The ordinarily skilled person would be able to reasonably extrapolate from the data in the application that any mutation at these positions which alters the encoded amino acid residue in the plexinB1 protein will have a similar effect.

One of ordinary skill in the art would therefore expect that all of the claimed mutants of plexin B1 were associated with cancer, in the light of the data set out in the specification, and thus an effect on the expression of these mutants would be predictably useful for identifying a compound as a putative anti-cancer agent.

For the reasons set out above, no undue experimentation would be required to practice the claimed invention.

Reconsideration and withdrawal of the Section 112, first paragraph "enablement", rejection are requested.

To the extent not obviated by the above amendments, the Section 112, first paragraph "written description", rejection of claims 106-111 is traversed. Reconsideration and withdrawal of the rejection are requested in view of the above and the following comments.

The claimed invention is described in the specification in a manner that one of ordinary skill will appreciate that the applicants were in possession of the claimed invention at the time the application was filed. The present claims relate to a sub-genus

of plexin B1 nucleic acids which contain a mutation located at one of a number of specified positions in the coding sequence of plexinB1 identified by reference to the sequence of database entry AB0007867.1.

The applicants submit that the description of plexinB1 mutations in the specification (e.g. Tables 1 and 2) adequately describes the claimed invention, since one example of a plexin B1 nucleic acid with a mutation at each position is disclosed. Furthermore, the applicants believe that since the mutations are located at specified sites in the plexinB1 sequence, the claimed invention does not include species which differ significantly in either structure or function from these examples.

The sites of mutation within the plexin B1 nucleic acids are identified by reference to the plexin B1 sequence of database entry AB0007867.1, so the positions of these mutations within the plexin B1 sequence can be readily determined.

The subject-matter of the present claims is therefore described in the specification such a way as to reasonably convey to one skilled in the relevant art that the inventors has possession of the claimed invention at the time the application was filed.

Reconsideration and withdrawal of the Section 112, first paragraph "written description", rejection are requested.

To the extent not obviated by the above amendments, the Section 102 rejection of claims 106-111 over Tang (WO0154477) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the above and the following comments.

The claimed invention relates to a plexin B1 nucleic acids which contain mutations located at one or more of a number of specified positions in the coding sequence of plexinB1 which are identified by reference to the sequence of database entry AB0007867.1. Because the positions of mutation are specified, the plexinB1 nucleic acids of these claims do not encompass nucleic acids which are completely distinct from plexinB1.

Tang is understood to disclose 1009 nucleotide sequences, including the sequence of plexin B1 (Table 2; page 123). This plexinB1 sequence (AJ011415.1) was publicly available on the Genbank database from 20 Sept 1999 onwards (i.e. before the earliest priority date of Tang).

Tang is silent regarding mutations in the plexinB1 sequence. In the absence of any teaching of the specific mutant plexin B1 nucleic acids of the present claims for example, Tang et al is not believed to teach each and every aspect of the claimed invention. The claims are submitted to be patentable over the cited art and withdrawal of the Section 102 rejection based on Tang is requested.

Furthermore, Tang fails to teach or suggest an association between plexinB1 or mutants thereof and cancer, in particular breast or prostate cancer. In the absence of such knowledge in the cited reference for example, Tang fails to literally or inherently teach the methods of the claimed invention to identify an anti-cancer agent.

Withdrawal of the Section 102 rejection based on Tang is requested.

To the extent not obviated by the above amendments, the Section 102 rejection of claims 106-111 over Mack (U.S. Patent Application Publication No. 2004/0005563) is

traversed. Reconsideration and withdrawal of the Section 102 rejection are requested in view of the above and the following further remarks.

The instant claims relate to a plexin B1 nucleic acids which contain mutations located at one or more of a number of specified positions in the coding sequence of plexinB1 which are identified by reference to the sequence of database entry AB0007867.1. Because the positions of mutation are specified, the plexinB1 nucleic acids of these claims do not encompass nucleic acids which are completely distinct from plexinB1.

Mack teaches that plexin B1 is one of many genes upregulated in ovarian cancer. Mack fails to literally or inherently teach mutations in the plexinB1 sequence, as presently claimed. Mack also fails to teach or suggest any relationship to breast and/or prostate cancer. In the absence of any teaching of the specific mutant plexin B1 nucleic acids of the present claims or breast or prostate cancer, for example, Mack fails to literally or inherently teach each and every aspect of the claimed invention.

Withdrawal of the Section 102 rejection of claims 106-111 over Mack is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned, preferably by telephone, in the event anything further is required in this regard.

Respectfully submitted,

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